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Mortality and Pulmonary Outcomes of Extremely Preterm Infants Exposed to Antenatal Corticosteroids

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Abstract

Background—Antenatal corticosteroids are given primarily to induce fetal lung maturation but results from meta-analyses of randomized controlled trials have not shown mortality or pulmonary benefits for extremely preterm infants although these are the infants most at risk of mortality and pulmonary disease.

Objective—We sought to determine if exposure to antenatal corticosteroids is associated with a lower rate of death and pulmonary morbidities by 36 weeks' postmenstrual age.

Study Design—Prospectively collected data on 11,022 infants 22 0/7 to 28 6/7 weeks' gestational age with a birth weight of 401 g and above born between January 1, 2006, and December 31, 2014 were analyzed. The rate of death and the rate of physiologic bronchopulmonary dysplasia by 36 weeks' postmenstrual age were analyzed by level of exposure to antenatal corticosteroids using models adjusted for maternal variables, infant variables, center, and epoch.

Results—Infants exposed to any antenatal corticosteroids had a lower rate of death [2193/9670 (22.7%)] compared to infants without exposure [540/1302 (41.5%)]; adjusted relative risk (ARR),

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0.71 (95% confidence interval (CI), 0.65 to 0.76; p<0.0001). Infants exposed to a partial course of antenatal corticosteroids also had a lower rate of death [654/2520 (26.0%)] compared to infants without exposure [540/1302 (41.5%); ARR, 0.77 (95% CI, 0.70 to 0.85); p<0.0001]. In an analysis by each week of gestation, infants exposed to a complete course of antenatal corticosteroids had lower mortality before discharge compared to infants without exposure at each week from 23 to 27 weeks' gestation and infants exposed to a partial course of antenatal corticosteroids had lower mortality at 23, 24, and 26 weeks' gestation. Rates of bronchopulmonary dysplasia in survivors did not differ by antenatal corticosteroid exposure. The rate of death due to respiratory distress syndrome, the rate of surfactant use, and the rate of mechanical ventilation were lower in infants exposed to any antenatal corticosteroids compared to infants without exposure.

Conclusion—Among infants 22–28 weeks' gestational age, any or partial antenatal exposure to corticosteroids compared to no exposure is associated with a lower rate of death while the rate of bronchopulmonary dysplasia in survivors did not differ.

Keywords

Antenatal corticosteroids; bronchopulmonary dysplasia; infant; mortality; morbidity; newborn; preterm; pulmonary; neonatal; respiratory distress syndrome; surfactant; mechanical ventilation; pneumothorax; pulmonary hemorrhage; sepsis; necrotizing enterocolitis; intracranial hemorrhage; periventricular leukomalacia; respiratory support; patent ductus arteriosus

INTRODUCTION

The effects of antenatal corticosteroids on mortality and pulmonary outcomes at the lowest gestations show mixed results, in part due to the small sample size of randomized controlled trials.[1,2] Although antenatal corticosteroids are given primarily to induce pulmonary maturity, induce surfactant release, and decrease respiratory distress syndrome, randomized controlled trials and meta-analyses of antenatal corticosteroids show no reduction in respiratory distress syndrome or neonatal death for infants delivered less than 30 weeks' gestation.[1,2] In addition, there are limited data from observational studies comparing the pulmonary outcomes of extremely preterm infants exposed to antenatal corticosteroids to those without exposure because these studies have not been focused on pulmonary outcomes.[3–8] Extremely preterm infants who die before 36 weeks' postmenstrual age cannot be assessed for the development of bronchopulmonary dysplasia, a type of chronic lung disease which is diagnosed at 36 weeks' postmenstrual age.[9] It is important to evaluate the competing outcomes of bronchopulmonary dysplasia and death both together and separately. Antenatal corticosteroid exposure may affect both outcomes for example if more infants survive following exposure and then develop bronchopulmonary dysplasia subsequently.

A complete course of antenatal corticosteroids is defined as two intramuscular doses of betamethasone given 12 to 24 hours apart or four intramuscular doses of dexamethasone given 12 hours apart.[10] Many preterm infants are born prior to the administration of a complete course of antenatal corticosteroids.[11,12] There are insufficient data on mortality and pulmonary outcomes of extremely preterm infants born after exposure to either a complete or a partial course of antenatal corticosteroids. We hypothesized that the rates of death would be lower in infants exposed to antenatal corticosteroids. In addition, we

hypothesized that the rates of physiologic bronchopulmonary dysplasia or death would be lower in infants exposed to antenatal corticosteroids. This study was also designed to determine if exposure to a partial or a complete course of antenatal corticosteroids is associated with improved survival and pulmonary outcomes in extremely preterm infants.

MATERIALS AND METHODS

This was a hypothesis-driven study using data collected prospectively for the Neonatal Research Network Generic Database and Follow-up studies. These data included infants 22 0/7 to 28 6/7 weeks' gestation with a birth weight of 401 g and above born between January 1, 2006 and December 31, 2014 at any of the National Institute of Child Health and Human Development Neonatal Research Network centers. Maternal and neonatal socio-demographic and clinical data were collected from medical records by trained research personnel. Gestational age was determined by best obstetric estimate over best neonatal estimate.[13] Infants with congenital anomalies were included if they were resuscitated as these infants were less likely to have lethal anomalies. Infants who died in the first 12 hours after birth without delivery room resuscitation were excluded from the primary analysis to ensure that results were not affected by planned restriction of care but were included in a secondary analysis. The study protocol was approved by each center's institutional review board.

Definitions

Infants were considered exposed to antenatal corticosteroids if their mother had received one or more doses of either betamethasone or dexamethasone.[10] Mothers were considered to have received a complete course if they had received at least two doses and 24 hours had passed from the time the first dose of antenatal corticosteroids was given. Data on repeat courses of antenatal corticosteroids were not collected.[14] Data were collected using standardized definitions until death or discharge. Follow up data was collected using standardized definitions on eligible surviving infants at 18–22 months corrected gestational age. Bronchopulmonary dysplasia was defined based on respiratory support at 36 weeks' postmenstrual age using the physiologic definition which uses an oxygen reduction challenge test among eligible infants.[15] The physiologic definition has been shown to be more reliable and precise than the clinical definition of bronchopulmonary dysplasia[15] (defined as supplemental oxygen at 36 weeks' postmenstrual age) and has been used by the Neonatal Research Network since 2006. All other outcomes were based on standardized definitions as per the Generic Database of the Neonatal Research Network.[16] Cause of death was defined as the underlying proximate disease which initiated the series of events leading to death based on both clinical evidence and autopsy findings where available.[13]

Statistical Analysis

The primary outcome measure was death before discharge. A formal sample size and power estimate demonstrated that the sample size resulting from inclusion of all infants delivered between January 1, 2006 and December 31, 2014 would provide more than 95% power to detect an absolute difference of 4% centered around an overall event rate of 25%. All secondary outcome measures and analyses were pre-specified. All outcomes were analyzed

by level of exposure to antenatal corticosteroid; complete exposure, partial exposure, any (partial or complete) exposure, and no exposure. Differences in categorical variables were described using Fisher's exact test. Kruskal-Wallis test was used for continuous skewed variables. Robust Poisson regression analysis was performed for factors present at birth associated with pulmonary outcomes including birth weight, sex, multiple births, small for gestational age (less than the 10th centile), maternal variables (age, marital status, race, diabetes, rupture of membranes ≥ 24 hours, antepartum hemorrhage, and mode of delivery), center, and epoch (2006–2009, and 2010–2014).[17–19] There were 0.5% missing data for the primary outcome and 9.7% missing data for the follow-up outcomes at 18–22 months corrected gestational age. To ensure that results were not affected by missing data, multiple imputation analyses were additionally conducted for outcomes with more than 1% of data missing, or when there was an imbalance of missing data of more than 0.3% between groups. An additional analysis was also performed adjusting for chorioamnionitis (diagnosed by placental pathology). This separate analysis was not performed by each week of gestation. SAS software version 9.3 (SAS Institute Inc) was used for all statistical analyses. Odds ratios and 95% confidence intervals were estimated for binary outcomes with a two sided *p* value of less than 0.05 indicating statistical significance.

RESULTS

A total of 11,022 infants met the inclusion criteria of whom 9,715 (88.1%) were exposed to antenatal corticosteroids. The proportion of infants at each gestational age from 23 to 28 weeks exposed to antenatal corticosteroids increased over the study period (Figure 1). Mothers of infants exposed to antenatal corticosteroids were more likely to be White, delivered by cesarean section, with private health insurance. Infants exposed to antenatal corticosteroids had higher birth weight, longer gestational age, and were more likely to be small for gestational age, and the product of multiple births (Table 1).

Infants exposed to any antenatal corticosteroids had lower mortality before discharge [2193/9670 (22.7%)] compared to infants without exposure [540/1302 (41.5%); adjusted relative risk (ARR), 0.71 (95% CI, 0.65 to 0.76); p<0.0001] (Table 2). Infants exposed to a partial course of antenatal corticosteroids also had lower mortality before discharge compared to infants without exposure (Table S1 in the Supplementary Appendix). In the analysis by each week of gestation, infants exposed to a complete course of antenatal corticosteroids had lower mortality before discharge compared to infants without exposure at each week from 23 to 27 weeks' gestation (Table 3, Figure 2). Infants exposed to a partial course of antenatal corticosteroids had lower mortality at 23, 24, and 26 weeks' gestation (Table 3, Figure 2).

Infants exposed to any antenatal corticosteroids had a lower rate of physiologic bronchopulmonary dysplasia or death by 36 weeks' postmenstrual age [6,016/9,579 (62.8%)] compared to infants without exposure [940/1,300 (72.3%)]; ARR, 0.94 (95% CI, 0.91 to 0.98); p=0.001] (Table 2). The rate of physiologic bronchopulmonary dysplasia or death by 36 weeks' postmenstrual age did not differ among infants exposed to a partial course of antenatal corticosteroids compared to infants without exposure (Table S1 in the Supplementary Appendix). The rate of physiologic bronchopulmonary dysplasia among

survivors at 36 weeks' postmenstrual age did not differ significantly in infants exposed to any antenatal corticosteroids compared to infants without exposure (Table 2). The rate of death due to bronchopulmonary dysplasia did not differ significantly in infants exposed to any antenatal corticosteroids [172/9661 (1.8%)] compared to infants without exposure [16/1299 (1.2%)]; ARR, 1.65 (95% CI, 0.96 to 2.83); p=0.068].

The rate of respiratory distress syndrome did not differ in infants exposed to any antenatal corticosteroids compared to infants without exposure (Table 2). The rate of death due to respiratory distress syndrome was lower in infants exposed to any antenatal corticosteroids compared to infants without exposure (Table 2). The rate of death due to respiratory distress syndrome was also lower in infants exposed to a complete or partial course of antenatal corticosteroids compared to infants without exposure (Table S1 in Supplementary Appendix). The rate of surfactant use and the rate of mechanical ventilation were lower in infants exposed to any antenatal corticosteroids compared to infants without exposure (Table 2).

Infants exposed to any antenatal corticosteroids had a lower rate of severe intracranial hemorrhage/periventricular leukomalacia and severe retinopathy of prematurity compared to infants without exposure (Table 2). The rate of pulmonary hemorrhage, pneumothorax, early onset sepsis, proven necrotizing enterocolitis, patent ductus arteriosus treated with indomethacin/ibuprofen, treatment with postnatal steroids for bronchopulmonary dysplasia, and prolonged hospital stay did not differ by antenatal corticosteroids exposure (Table 2). Among survivors exposed to any antenatal corticosteroids there was a higher rate of oxygen therapy at discharge compared to infants without exposure but among survivors who were followed at 18–22 months' corrected age, the rate of oxygen therapy and continuous positive airway pressure/ventilator did not differ by antenatal corticosteroid exposure (Table 2).

Infants exposed to a complete course of antenatal corticosteroids had a lower rate of death before discharge compared to infants exposed to a partial course of antenatal corticosteroids (Table S1 in the Supplementary Appendix). Infants exposed to a complete course of antenatal corticosteroids also had a lower rate of death due to respiratory distress syndrome, surfactant use, mechanical ventilation, severe intracranial hemorrhage/periventricular leukomalacia, and pulmonary hemorrhage compare to infants exposed to a partial course of antenatal corticosteroids (Table S1 in the Supplementary Appendix).

The inclusion of the 883 infants who died within 12 hours without receiving delivery room resuscitation strengthened the association between lower mortality and exposure to antenatal corticosteroids, particularly among infants at the lowest gestations (Table S2 in the Supplementary Appendix). The results of the models using multiple imputation for missing data were substantively similar to the primary analysis (Table S3 in the Supplementary Appendix). The results of the models that included chorioamnionitis did not substantively differ and are not presented.

COMMENT

Principal Findings

This large multicenter observational study shows that exposure to a complete or partial course of antenatal corticosteroids is associated with lower mortality in infants 22 to 28 weeks' gestation and weighing 401 grams and above after adjustment for multiple confounders. Among survivors, the rate of bronchopulmonary dysplasia in infants exposed to either a complete or partial course of antenatal corticosteroids did not differ compared to infants who were not exposed. Although all groups had a high rate of respiratory distress syndrome, there was a lower rate of death due to respiratory distress syndrome and a lower use of surfactant and mechanical ventilation among infants exposed to antenatal corticosteroids indicating amelioration of the course of respiratory distress syndrome.

Meaning/clinical implications of findings

The current study demonstrates a lower rate of death associated with exposure to antenatal corticosteroids in infants less than 29 weeks' gestation. Randomized controlled trials of administration of antenatal corticosteroids to women who delivered at less than 30 weeks' gestation show inconclusive neonatal outcomes, in part due to small sample size.[1–2] In the Cochrane review subgroup analysis of those infants less than 28 weeks' gestation, there was no significant reduction in the rate of neonatal death but the sample was small [two studies, 89 infants]. The current study agrees with data from observational studies which show a survival benefit among extremely preterm infants at the lowest gestations.[20]

Many of the studies included in the meta-analyses of randomized controlled trials[1–2] were carried out in the era before the widespread use of surfactant and when the methods of ventilatory support used were different.[21–22] In the Cochrane review subgroup analysis of those infants less than 28 weeks' gestation, there was no significant reduction in the rate of respiratory distress syndrome [four studies, 102 infants].[1] Rates of bronchopulmonary dysplasia were not analyzed by gestational age at delivery but were not different for the cohort as a whole [six studies, 818 infants]. In the current study, the rates of respiratory distress syndrome and the rates of bronchopulmonary dysplasia among survivors were also not different.

Observational studies have shown marked variability in pulmonary outcomes in infants at the lowest gestations. A NICHD Neonatal Research Network study including 10,541 infants delivered between 22 and 25 weeks' gestation, found that a lower mortality rate associated with exposure to antenatal corticosteroids was partially offset by a higher rate of bronchopulmonary dysplasia among survivors compared to infants without exposure.[3] A multicenter study of 2,549 infants less than 29 weeks' gestation also found that the rate of bronchopulmonary dysplasia was higher in infants exposed to a complete course of antenatal corticosteroids compared to infants without exposure.[4] Another multicenter study of 11,607 infants born 22 to 33 weeks' gestation found that the rates of bronchopulmonary dysplasia did not differ in infants exposed to any antenatal corticosteroids compared to infants without exposure.[5] These differences in bronchopulmonary dysplasia rates may be related to the different definition of bronchopulmonary dysplasia[9] used in these studies as well as the

gestational age inclusion criteria as inclusion of infants at the lowest gestations would result in more survivors who can develop bronchopulmonary dysplasia.

An important focus of the current study was the differential benefits of a partial or a complete course of antenatal corticosteroids. Although a complete course of antenatal corticosteroids is associated with a lower mortality compared to a partial course, the current study indicates that the first dose of antenatal corticosteroids may have the largest effect on reducing mortality. The Cochrane review of randomized controlled trials subgroup analysis of infants delivered following a partial course of antenatal corticosteroids showed a significant reduction in neonatal death in infants exposed to a partial course [four studies, 295 infants].[1] The current study results are in concordance with those of an observational study of 9,949 infants weighing 501 to 1500 grams from the era before widespread use of antenatal corticosteroids and surfactant which found a lower rate of death before discharge in infants exposed to a partial course of antenatal corticosteroids compared to infants without exposure.[6] In that study the rate of bronchopulmonary dysplasia also did not differ by degree of exposure to antenatal corticosteroids. The aforementioned study by Wong et al indicated that mortality did not differ in infants exposed to a partial course of antenatal corticosteroids compared to infants without exposure but this study was limited by a relatively small sample size.[4]

Strengths & Weaknesses

This study used data collected from top academic centers across the United States where optimal obstetric and neonatal care might be anticipated but there are several limitations which should be noted. There was no inception cohort of fetuses exposed or not exposed to antenatal corticosteroids. Data were not available on the exact timing of antenatal corticosteroids, whether fetal monitoring was undertaken prior to delivery, or the length of maternal hospitalization before delivery.[23] There is a risk of bias as women admitted in advanced labor most likely would be overrepresented in the group that did not receive antenatal corticosteroids. While it is also unlikely that the results of this study are only due to confounding, there may be some residual unmeasured bias in the results due to baseline differences between the study groups which may not be adequately adjusted for in the models used. In addition, there is a possibility of postnatal bias in which infants not exposed to antenatal corticosteroids may have had their care restricted or withheld, particularly among infants at the lowest gestations. To reduce this effect, infants who died within 12 hours of birth without receiving delivery room resuscitation were excluded from the primary analysis. The multiple testing used in this study at a 5% significance level may have resulted in a few results being significant purely by chance. However, the benefits were consistent at most gestations, suggesting that the results are not only due to chance.

Research implications

Although antenatal corticosteroid administration reduces preterm infant mortality and morbidity without increasing the cost of care,[1] many eligible women[24] do not receive this treatment.[11,12] Center differences in the use of antenatal corticosteroids are associated with mortality among infants at the lowest gestations.[25,26] Differences between administration

rates among infants by gestation in this study indicate that although administration rates are increasing, there are opportunities for quality improvement.[26]

Conclusion

The current study demonstrates that antenatal exposure to corticosteroids for infants 22 0/7 to 28 6/7 weeks' gestation is associated with a lower rate of death before discharge without a higher rate of bronchopulmonary dysplasia or other major adverse pulmonary problems. This study also indicates that antenatal corticosteroids ameliorate the severity of respiratory distress syndrome and other important morbidities in extremely preterm infants.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Roberts D, Dalziel S. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. Cochrane Database Syst Rev. 2006; 3:CD004454.
2. Onland W, de Laat MW, Mol BW, Offringa M. Effects of antenatal corticosteroids given prior to 26 weeks' gestation: a systematic review of randomized controlled trials. Am J Perinatol. 2011; 28(1): 33–44. [PubMed: 20648416]
3. Carlo WA, McDonald SA, Fanaroff AA, et al. for the NICHD Neonatal Research Network. Association of antenatal corticosteroids with mortality and neurodevelopmental outcomes among infants born at 22 to 25 weeks' gestation. JAMA. 2011; 306(21):2348–58. [PubMed: 22147379]
4. Wong D, Abdel-Latif M, Kent A, NICUS Network. Antenatal steroid exposure and outcomes of very premature infants: a regional cohort study. Arch Dis Child Fetal Neonatal Ed. 2014; 99(1):F12–20. [PubMed: 24142624]
5. Mori R, Kusuda S, Fujimura M, Neonatal Research Network. Antenatal corticosteroids promote survival of extremely preterm infants born at 22 to 23 weeks of gestation. J Pediatr. 2011; 159(1): 110–114. [PubMed: 21334006]
6. Wright LL, Verter J, Younes N, et al. Antenatal corticosteroid administration and neonatal outcome in very low birth weight infants: the NICHD Neonatal Research Network. Am J Obstet Gynecol. 1995; 173(1):269–274. [PubMed: 7631702]
7. Manktelow BN, Lal MK, Field DJ, Sinha SK. Antenatal corticosteroids and neonatal outcomes according to gestational age: a cohort study. Arch Dis Child Fetal Neonatal Ed. 2010; 95(2):F95–8. [PubMed: 19948527]
8. Doyle LW, Kitchen WH, Ford GW, Rickards AL, Kelly EA. Antenatal steroid therapy and 5-year outcome of extremely low birth weight infants. Obstetrics and gynecology. 1989; 73(5 Pt 1):743–746. [PubMed: 2704500]
9. Jobe AH, Bancalari E. Bronchopulmonary dysplasia. Am J Respir Crit Care Med. 2001; 163(7): 1723–9. [PubMed: 11401896]
10. Brownfoot FC, Gagliardi DI, Bain E, Middleton P, Crowther CA. Different corticosteroids and regimens for accelerating fetal lung maturation for women at risk of preterm birth. Cochrane Database Syst Rev. 2013; 8:CD006764.
11. Davidson C, Monga M, Ellison D, Vidaeff A. Continuation of pregnancy after antenatal corticosteroid administration: opportunity for rescue? J Reprod Med. 2010; 55(1–2):14–8. [PubMed: 20337202]
12. Melamed N, Shah J, Soraisham A, et al. Association between antenatal corticosteroid administration-to-birth interval and outcomes of preterm neonates. Obstet Gynecol. 2015; 125(6): 1377–84. [PubMed: 26000509]
13. Patel RM, Kandefer S, Walsh MC, et al. for the Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network. Causes and timing of death in extremely premature infants from 2000 through 2011. N Engl J Med. 2015; 372(4):331–40. [PubMed: 25607427]
14. McKinlay CJ, Crowther CA, Middleton P, Harding JE. Repeat antenatal glucocorticoids for women at risk of preterm birth: a Cochrane Systematic Review. Am J Obstet Gynecol. 2012; 206(3):187–94. [PubMed: 21982021]
15. Walsh MC, Wilson-Costello D, Zadell A, Newman N, Fanaroff A. Safety, reliability, and validity of a physiologic definition of bronchopulmonary dysplasia. J Perinatol. 2003; 23(6):451–6. [PubMed: 13679930]
16. Stoll BJ, Hansen NI, Bell EF, et al. for the NICHD Neonatal Research Network, Trends in Care Practices, Morbidity, and Mortality of Extremely Preterm Neonates, 1993–2012. JAMA. 2015; 314(10):1039–51. [PubMed: 26348753]
17. Tyson JE, Parikh NA, Langer J, Green C, Higgins RD. Intensive care for extreme prematurity–moving beyond gestational age. N Engl J Med. 2008; 358(16):1672–1681. [PubMed: 18420500]

18. Ambalavanan N, Van Meurs KP, Perritt R, et al. for the NICHD Neonatal Research Network. Predictors of death or bronchopulmonary dysplasia in preterm infants with respiratory failure. J Perinatol. 2008; 28(6):420–6. [PubMed: 18337740]

19. Haas DM, Sischy AC, McCullough W, Simsiman AJ. Maternal ethnicity influences on neonatal respiratory outcomes after antenatal corticosteroid use for anticipated preterm delivery. J Matern Fetal Neonatal Med. 2011; 24(3):516–20. [PubMed: 20672908]

20. Park CK, Isayama T, McDonald SD. Antenatal Corticosteroid Therapy Before 24 Weeks of Gestation: A Systematic Review and Meta-analysis. Obstet Gynecol. 2016; 127(4):715–25. [PubMed: 26959200]

21. Fischer HS, Bührer C. Avoiding endotracheal ventilation to prevent bronchopulmonary dysplasia: a meta-analysis. Pediatrics. 2013; 132(5):1351–60.

22. St John EB, Carlo WA. Respiratory distress syndrome in VLBW infants: changes in management and outcomes observed by the NICHD Neonatal Research Network. Semin Perinatol. 2003; 27:288–292. [PubMed: 14510319]

23. Bottoms SF, Paul RH, Iams JD, et al. for the National Institute of Child Health and Human Development Network of Maternal-Fetal Medicine Units. Obstetric determinants of neonatal survival: influence of willingness to perform cesarean delivery on survival of extremely low-birth-weight infants. Am J Obstet Gynecol. 1997; 176(5):960–6. [PubMed: 9166152]

24. Raju TN, Mercer BM, Burchfield DJ, Joseph GF Jr. Periviable birth: executive summary of a joint workshop by the Eunice Kennedy Shriver National Institute of Child Health and Human Development, Society for Maternal-Fetal Medicine, American Academy of Pediatrics, and American College of Obstetricians and Gynecologists. Am J Obstet Gynecol. 2014; 210(5):406–17. [PubMed: 24725732]

25. Smith PB, Ambalavanan N, Li L, et al. for the Eunice Kennedy Shriver National Institute of Child Health Human Development Neonatal Research Network. Approach to infants born at 22 to 24 weeks' gestation: relationship to outcomes of more-mature infants. Pediatrics. 2012; 129(6):1508–16.

26. Rysavy MA, Li L, Bell EF, et al. for the Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network. Between-hospital variation in treatment and outcomes in extremely preterm infants. N Engl J Med. 2015; 372(19):1801–11. [PubMed: 25946279]

Condensation

Exposure to antenatal corticosteroids is associated with a lower rate of death which is not offset by a higher rate of bronchopulmonary dysplasia.

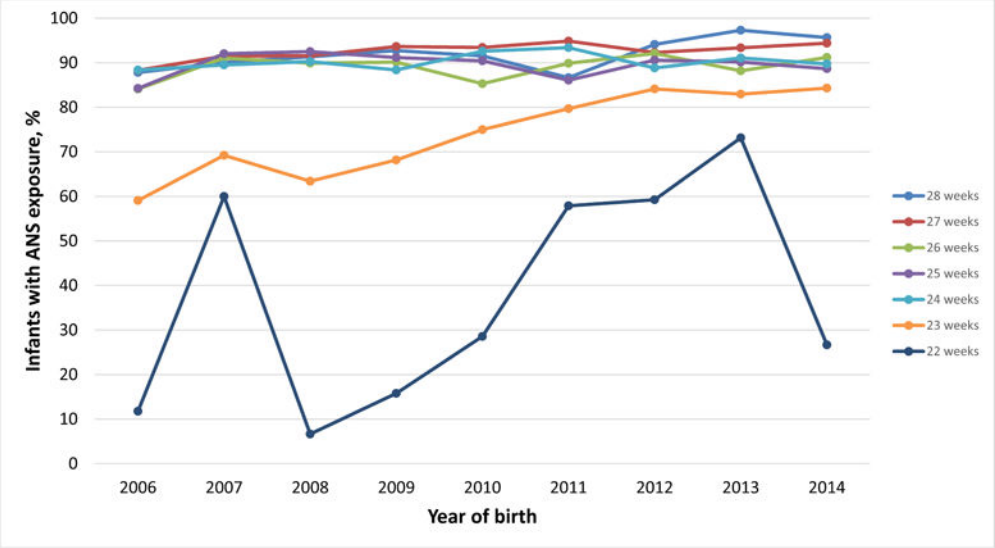

Figure 1.

Frequency of exposure to antenatal corticosteroids (ANS) by gestational age and year of birth. The administration of antenatal corticosteroids increased over the study period but remained lower at the lower gestational ages.

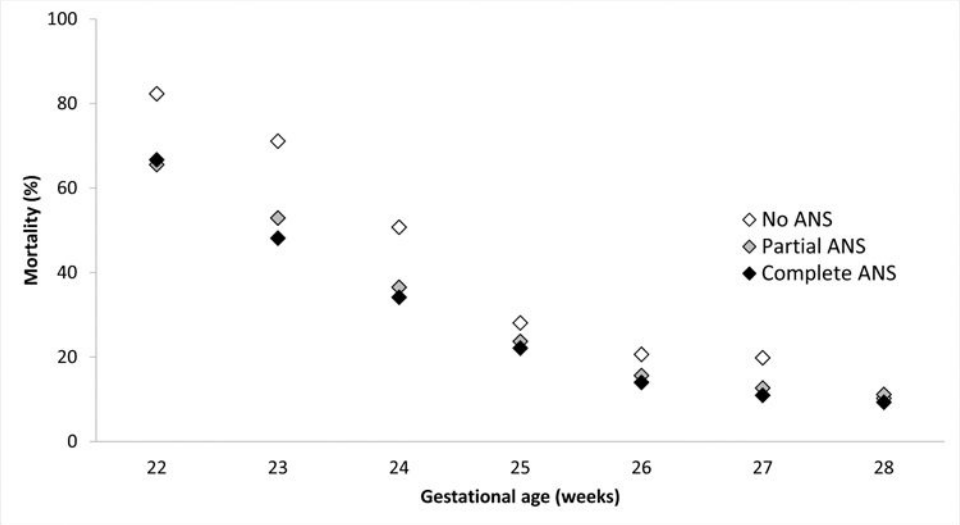

Figure 2.

Death before discharge of infants 22 to 28 weeks' gestation by antenatal corticosteroid (ANS) exposure. Infants exposed to a course of antenatal corticosteroids had a lower rate of death before discharge compared to infants who were not exposed to antenatal corticosteroids at each gestational age from 23 to 27 weeks. Infants exposed to a partial course of antenatal corticosteroids had lower mortality at 23, 24, and 26 weeks' gestation.

Table 1

Infant/maternal baseline characteristics by antenatal corticosteroid treatment

	Any ANS	No ANS
Study population, n	9715	1307
Mother		
Maternal race/ethnicity		
Black (including Black Hispanic)	3893 (40.9)[a]	663 (52.0)[a]
White (including White Hispanic)	5066 (53.3)[a]	546 (42.8)[a]
Other	550 (5.8)[a]	66 (5.2)[a]
All Hispanic	1366 (14.5)[a]	288 (22.7)[a]
Maternal health insurance		
Medicaid	5096 (52.8)[a]	807 (62.4)[a]
Private insurance	4072 (42.2)[a]	355 (27.5)[a]
Self-pay/uninsured	480 (5.0)[a]	131 (10.1)[a]
Infant		
Birth weight, g	748 ± 148[a]	719 ± 155[a]
Gestational age, wk	25.5 ± 1.5[a]	24.8 ± 1.7[a]
Male sex	4731 (48.7)	668 (51.1)
Multiple births	2565 (26.4)[a]	285 (21.8)[a]
Small for gestational age	1078 (11.1)[a]	99 (7.6)[a]
Caesarean delivery	6697 (68.9)[a]	743 (56.9)[a]

Values are n (%) or ± SD.

ANS, antenatal corticosteroid.

[a]Significant with P value <.05 for comparisons of ANS vs no ANS data.

Table 2

Outcomes of infants by exposure to antenatal corticosteroids

	Any ANS n/total n (%)	No ANS n/total n (%)	ARR (95% CI)[a]
Total study population	N=9715	N=1307	
Death			
By 36 wk' postmenstrual age	1952/9692 (20.1)	513/1305 (39.3)	0.67 (0.62 – 0.73)[b]
Before discharge	2193/9670 (22.7)	540/1302 (41.5)	0.71 (0.65 – 0.76)[b]
Due to bronchopulmonary dysplasia	172/9661 (1.8)	16/1299 (1.2)	1.65 (0.96 – 2.83)[c]
Due to respiratory distress syndrome	698/9661 (7.2)	171/1299 (13.2)	0.72 (0.60 – 0.86)[b,c]
Bronchopulmonary dysplasia (physiologic definition) or death by 36 wk' postmenstrual age	6016/9579 (62.8)	940/1300 (72.3)	0.94 (0.91 – 0.98)[b]
Population of survivors	N=7477	N=762	
Bronchopulmonary dysplasia, physiologic definition	3810/7359 (51.8)	396/755 (52.5)	0.96 (0.89 – 1.03)
Bronchopulmonary dysplasia, by use of supplemental oxygen at 36 wk' postmenstrual age, clinical definition	3999/7431 (53.8)	415/759 (54.7)	0.96 (0.90 – 1.03)
Respiratory distress syndrome	7367/7477 (98.5)	760/762 (99.7)	0.99 (0.99 – 1.00)
Surfactant use	6347/7477 (84.9)	702/762 (92.1)	0.92 (0.89 – 0.94)[b]
Mechanical ventilation	6742/7472 (90.2)	723/762 (94.9)	0.96 (0.94 – 0.98)[b]
Pneumothorax	354/7477 (4.7)	45/762 (5.9)	0.78 (0.56 – 1.08)[c]
Pulmonary hemorrhage	305/7477 (4.1)	47/762 (6.2)	0.75 (0.55 – 1.03)[c]
Treatment with post-natal steroids for bronchopulmonary dysplasia	1218/7268 (16.8)	112/733 (15.3)	0.98 (0.82 – 1.18)
Early onset sepsis	134/7477 (1.8)	17/762 (2.2)	0.67 (0.40 – 1.13)[c]
Necrotizing enterocolitis ≥ stage 2	668/7476 (8.9)	71/762 (9.3)	0.98 (0.77 – 1.26)[c]
Intracranial hemorrhage/periventricular leukomalacia	1028/7445 (13.8)	167/761 (21.9)	0.66 (0.57–0.77)[b,c]
Patent ductus arteriosus treated with indomethacin/ibuprofen	2454/7471 (32.8)	293/761 (38.5)	0.95 (0.86 – 1.05)
Retinopathy of prematurity ≥ stage 3 or treated with ablation/anti-VEGF drug	1325/7342 (18.0)	178/753 (23.6)	0.76 (0.66 – 0.87)[b,c]
Respiratory support at discharge, oxygen	2386/7216 (33.1)	195/740 (26.4)	1.17 (1.03 – 1.33)[b,c]
Prolonged hospital stay ≥ 120 d, all causes	2086/7315 (28.5)	235/752 (31.3)	0.94 (0.84 – 1.05)
Population of survivors eligible for follow-up	N=4149	N=471	
Respiratory support at 18–22 mo corrected age, ventilation/CPAP	67/3749 (1.8)	7/422 (1.7)	0.91 (0.42 – 1.99)[c]
Oxygen at 18–22 mo corrected age	201/3749 (5.4)	20/422 (4.7)	1.01 (0.65 – 1.58)[c]

ANS, antenatal corticosteroid; ARR, adjusted relative risk; CI, confidence interval; CPAP, continuous positive airway pressure; VEGF, vascular endothelial growth factor.

[a] ARR and 95% CI are estimated with no ANS (not exposed to ANS) group used as referent category except for complete vs partial column where ARR and 95%CI are expressed for complete course of ANS compared to partial course of ANS-models adjust for birthweight, sex, multiple births, small for gestational age, maternal variables (age, marital status, race, diabetes, rupture of membranes >24 h, antepartum hemorrhage, and mode of delivery), center, and epoch

[b] Significant with P value <.05

[c] Model does not adjust for center-model did not converge with center included.

Table 3

Selected outcomes of infants 22–28 weeks' gestation by antenatal corticosteroid treatment for births from 2006 through 2014

	Complete ANS		Partial ANS		No ANS
	n/total n (%)	ARR (95% CI)[a]	n/total n (%)	ARR (95% CI)	n/total n (%)
Bronchopulmonary dysplasia, physiologic, or death by 36 wk' postmenstrual age					
22 wk	45/48 (93.8)	0.95 (0.86–1.05)	27/28 (96.4)	0.96 (0.88–1.05)	94/96 (97.9)
23 wk	437/508 (86.0)	0.89 (0.84–0.94)[b]	282/312 (90.4)	0.98 (0.93–1.02)	264/281 (94.0)
24 wk	1100/1390 (79.1)	0.95 (0.87–1.03)	404/499 (81.0)	1.03 (0.94–1.12)	166/208 (79.8)
25 wk	1043/1581 (66.0)	0.93 (0.84–1.02)[c]	374/572 (65.4)	0.94 (0.84–1.05)	163/250 (65.2)
26 wk	835/1483 (56.3)	0.93 (0.83–1.04)[c]	283/495 (57.2)	0.97 (0.84–1.11)	144/245 (58.8)
27 wk	592/1243 (47.6)	0.86 (0.72–1.02)[c]	159/367 (43.3)	0.84 (0.69–1.03)[c]	74/132 (56.1)
28 wk	330/781 (42.3)	0.98 (0.75–1.27)[c]	85/231 (36.8)	0.88 (0.64–1.20)[c]	35/88 (39.8)
Death by 36 wk' postmenstrual age					
22 wk	31/48 (64.6)	0.79 (0.61–1.04)[c]	19/29 (65.5)	0.85 (0.64–1.14)[c]	78/97 (80.4)
23 wk	226/509 (44.4)	0.68 (0.59–0.78)[b,c]	156/314 (49.7)	0.77 (0.67–0.88)[b,c]	194/281 (69.0)
24 wk	441/1409 (31.3)	0.54 (0.45–0.64)[b,c]	170/504 (33.7)	0.75 (0.60–0.93)[b]	99/209 (47.4)
25 wk	310/1596 (19.4)	0.66 (0.51–0.85)[b,c]	122/576 (21.2)	0.76 (0.58–0.99)[b,c]	68/253 (26.9)
26 wk	176/1499 (11.7)	0.55 (0.40–0.76)[b,c]	69/499 (13.8)	0.64 (0.45–0.92)[b,c]	47/247 (19.0)
27 wk	112/1262 (8.9)	0.60 (0.37–0.98)[b,c]	37/372 (9.9)	0.73 (0.42–1.27)[c]	20/130 (15.4)
28 wk	56/796 (7.0)	0.82 (0.39–1.74)[c]	18/233 (7.7)	0.75 (0.30–1.87)[c]	7/88 (8.0)
Death before discharge					
22 wk	32/48 (66.7)	0.83 (0.64–1.07)[c]	19/29 (65.5)	0.83 (0.63–1.10)[c]	79/96 (82.3)
23 wk	243/505 (48.1)	0.72 (0.63–0.82)[b,c]	164/310 (52.9)	0.80 (0.70–0.91)[b,c]	199/280 (71.1)
24 wk	480/1406 (34.1)	0.57 (0.48–0.67)[b,c]	184/504 (36.5)	0.75 (0.61–0.91)[b]	105/207 (50.7)
25 wk	352/1592 (22.1)	0.75 (0.59–0.95)[b,c]	136/574 (23.7)	0.83 (0.64–1.07)[c]	71/253 (28.1)
26 wk	210/1498 (14.0)	0.61 (0.45–0.82)[b,c]	78/499 (15.6)	0.67 (0.48–0.94)[b,c]	51/247 (20.6)

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	Complete ANS		Partial ANS		No ANS
	n/total n (%)	ARR (95% CI)[a]	n/total n (%)	ARR (95% CI)	n/total n (%)
27 wk	138/1260 (11.0)	0.58 (0.38–0.87)[b,c]	47/371 (12.7)	0.70 (0.44–1.13)[c]	26/131 (19.8)
28 wk	74/795 (9.3)	0.86 (0.44–1.67)[c]	26/233 (11.2)	1.06 (0.49–2.27)[c]	9/88 (10.2)
Bronchopulmonary dysplasia, physiologic definition					
22 wk	13/16 (81.3)	0.64 (0.35–1.16)	8/9 (88.9)	0.96 (0.82–1.11)[c]	15/16 (93.8)
23 wk	191/261 (73.2)	0.80 (0.68–0.94)[b,c]	114/144 (79.2)	0.97 (0.83–1.12)[c]	64/81 (79.0)
24 wk	619/907 (68.2)	1.09 (0.92–1.30)[c]	220/315 (69.8)	1.18 (0.98–1.41)	59/101 (58.4)
25 wk	690/1224 (56.4)	0.96 (0.83–1.12)[c]	235/434 (54.1)	0.95 (0.81–1.12)	92/179 (51.4)
26 wk	622/1268 (49.1)	0.99 (0.85–1.15)[c]	206/417 (49.4)	0.95 (0.80–1.12)[c]	93/194 (47.9)
27 wk	454/1103 (41.2)	0.94 (0.74–1.19)[c]	111/319 (34.8)	0.87 (0.66–1.15)[c]	47/105 (44.8)
28 wk	258/706 (36.5)	1.02 (0.74–1.42)[c]	59/205 (28.8)	0.83 (0.56–1.22)[c]	26/79 (32.9)
Respiratory support at discharge, oxygen					
22 wk	13/16 (81.3)	*d*	6/10 (60.0)	0.52 (0.23–1.18)[c]	9/14 (64.3)
23 wk	150/258 (58.1)	1.04 (0.78–1.39)[c]	82/140 (58.6)	*d*	36/77 (46.8)
24 wk	407/892 (45.6)	1.26 (0.94–1.69)[c]	134/309 (43.4)	1.17 (0.86–1.60)[c]	34/101 (33.7)
25 wk	434/1196 (36.3)	1.06 (0.83–1.36)[c]	158/431 (36.7)	1.22 (0.92–1.60)[c]	50/179 (27.9)
26 wk	352/1238 (28.4)	1.21 (0.90–1.62)[c]	124/409 (30.3)	1.23 (0.90–1.68)[c]	44/191 (23.0)
27 wk	278/1077 (25.8)	1.39 (0.90–2.13)[c]	63/317 (19.9)	1.22 (0.74–2.03)[c]	18/101 (17.8)
28 wk	144/688 (20.9)	3.62 (1.38–9.46)[c]	38/202 (18.8)	*d*	4/77 (5.2)

ANS, antenatal corticosteroid; ARR, adjusted relative risk; CI, confidence interval.

[a]ARR and 95% CI are estimated with no ANS (not exposed to ANS) group used as referent category-models adjust for birthweight, sex, multiple births, small for gestational age, maternal variables (age, marital status, race, diabetes, rupture of membranes >24 h, antepartum hemorrhage, and mode of delivery), center, and epoch

[b]Significant with P value <.05

[c]Model does not adjust for center-model did not converge with center included

[d]Model did not converge even with center excluded-for respiratory support at discharge (oxygen): unadjusted relative risks (95% CI) for complete ANS at 22 wk: 1.26 (0.80-1.99); for partial ANS at 23 wk: 1.25 (0.95-1.65); and for partial ANS at 28 wk: 3.62 (1.34-9.81).